

REMARKS*Status of the Claims*

Upon entry of these remarks claims 75, 79, 81, 82, 87-89, and 97-145 will be pending. Claims 1-74, 76-78, 80, 83-86, and 90-96 have been cancelled without prejudice or disclaimer. New claims 97-145, which correspond to provisionally elected Group I (cancelled claims 1-74, 80, and 83-86 and pending claims 81 and 82) have been added. Support for the newly added claims is found throughout the specification and claims as originally filed, and no new matter has been introduced.

More particularly, support for new claims directed to antibodies of the invention can be found, for example, in the originally filed claims. Additional support for the new claims may be found, for example, in paragraphs [0282]-[0290], [0293], [0294] and Example 16 (antibodies that competitively inhibit the binding of the antibody produced by ATCC Deposit PTA-3239 or PTA-3240); in paragraphs [031], [0243], [0244] and Table 1 on page 296, line 10 (antibodies that immunospecifically bind BLyS comprising a fragment or variant of a fragment of the scFv of SEQ ID NO:327); in paragraphs [026] and [027] (types of antibodies, i.e. monoclonal, scFv, chimeric, Fab, etc.); in paragraphs [027] and [0273] (antibodies comprising constant domains); in paragraph [0245] (antibodies with a  $K_D$  less than or equal to  $10^{-9}$  M); in paragraphs [0327] and [0342] (antibodies coupled to a detectable label); in paragraphs [060]-[063] (antibodies that bind multimeric forms of BLyS); in paragraphs [0248]-[0250], [0327]-[0329] and Example 3 (antibodies that neutralize BLyS); in paragraphs [0277], [0278] and the Table between paragraphs [0274] and [0275] (antibodies purified from the cell line contained in either ATCC Deposit Number PTA-3239 or PTA-3240. Thus, no new matter has been added by way of amendment.

*can be derived from human lymphocytes*

**Provisional Election**

Preliminarily, Applicants note that certain portions of the written restriction requirement (Paper No. 7), particularly with respect to the required species elections, are contrary to Applicants' understanding of USPTO restriction practice. Applicants have made a good faith effort to be fully responsive to the Examiner's restriction requirement,

providing explanations when necessary as to why Applicants' provisional election is as responsive as possible.

The Examiner has required an election under 35 U.S.C. §121 of one of Groups I - VI (See, Paper No. 7, pages 2-3). As defined by the Examiner, the claims of Group I are drawn to an antibody that immunospecifically binds to BLYS and a kit comprising said antibody; the claims of Group II are drawn to an isolated nucleic acid molecule encoding an antibody, a vector and host cell respectively; the claims of Group III are drawn to a cell line engineered to express an antibody; the claims of Group IV are drawn to a method for detecting aberrant expression of BLYS protein; the claims of Group V are drawn to a method for diagnosing a disease or disorder associated with aberrant BLYS expression or activity; the claims of Group VI are drawn to a method of treating, preventing or ameliorating a disease associated with aberrant BLYS. Applicants elect Group I (cancelled claims 1-74, 80, and 83-86, currently amended claims 81 and 82, and new claims 97-145), *with traverse*. Applicants submit that the newly added claims fall within the scope of Group I as defined by the Examiner.

The Examiner has instructed that if Group I is elected, a sequence election must be made and an election of species from each of species sets A-H is required. Applicants make each of the following sequence election and species elections, *with traverse*:

Applicants elect the sequence of SEQ ID NO:327, *with traverse*.

From Group A, Applicants elect the I116A01 scFv species, *with traverse*. In paragraph 5, of the restriction requirement the Examiner requires that Applicants define the correspondence of the elected species from species set A to the above elected sequence. As indicated in Table 1 (more specifically on page 296, line 10), the amino acid sequence of scFv I116A01 is provided in SEQ ID NO:327.

From species set B, Applicants elect the "monoclonal antibody" species, *with traverse*.

From species set C, Applicants elect the "human IgG1 constant domain" species, *with traverse*.

From species set D, Applicants elect the "human Ig lambda constant domain" species, *with traverse*.

As discussed below, Applicants have written new claims corresponding to species set E, such that they only contain one species, thus obviating this species election requirement.

Applicants have cancelled the claim corresponding to species set F, thus obviating this species election requirement.

From species set G, Applicants elect TACI, *with traverse*.

Applicants have cancelled the claim corresponding to species set H, thus obviating this species election requirement.

Paragraph 22 of the restriction requirement instructs that in addition to making a sequence election and species election from each of species sets A-H, Applicants must provide a "listing of all claims readable thereon, including any claims subsequently added." The following chart indicates which claims correspond to Group I and to each required species election:

<u>Group or Species Set</u>	<u>Pending "claims readable thereon"</u>
Group I	81, 82 and 97 <sup>1</sup> -145
Sequence Election	81, 82 and 97 <sup>1</sup> -145
Species Set A	81, 82 and 97 <sup>1</sup> -145
Species Set B	102-104, 119-121, and 136-138; Claims 103, 120 and 137 encompass the elected species <sup>2</sup>
Species Set C	105, 122, 139
Species Set D	106, 123, 140
Species Set E	107 and 124
Species Set F	None
Species Set G	115-116 and 130-131
Species Set H	None

In the preceding, Applicants have attempted to be fully responsive to the Examiner's restriction requirement. However, Applicants fervently request reconsideration and withdrawal or modification of the present restriction requirement. The following discussion expounds upon Applicants reasons for asserting that the present

<sup>1</sup> Applicants assert claim 97 is a generic linking claim and should be removed from Group I and examined separately with the elected Group according to MPEP procedure for the examination of linking claims (discussed below).

<sup>2</sup> The original Markush group of claim 48 (on which species election B is based), contained multiple members. In newly added claims corresponding to original Markush group of claim 48, certain members of the Markush group have been eliminated or broken out into individual dependent claims (see claims 103-104, 120-121, and 137-138).

restriction requirement is improper, and should be withdrawn or, at the very least, modified.

### Traversal of Provisional Election

Prior to Applicants' explanation of their grounds for traversing the restriction requirement set forth in Paper No. 7, Applicants wish to make certain comments regarding (1) the required sequence election, particularly as it compares to the required species election from species set A, and (2) Applicants' presentation of claims corresponding to original Markush claim 51 (i.e., pending claims 107 and 124).

#### *Sequence Election*

(a) *Sequence Election vs. Species Election from Species Set A.* Preliminarily, Applicants have elected SEQ ID NO:327 as the "sequence election" and have elected scFv I116A01 to meet the requirement for an election of species from species set A. Applicants do not see a distinction between these two requirements. Perhaps these two requirements were made in the absence of the knowledge that each of SEQ ID NOS:1-2128 corresponds to a unique scFv amino acid sequence. The relationship of every scFv to its sequence identifier is made clear in Table 1 which spans pages 287-246 of the specification as filed. Having made this clarification, Applicants respectfully request that the Examiner reconsider and withdraw the requirement for a species election from species set A, as such an election would be redundant to the requirement for a sequence election.

(b) *Traversal of Sequence Election.* Applicants have elected the sequence of SEQ ID NO:327, with the following traverse. Section 803.04 of the MPEP states that

Nucleotide sequences encoding different proteins are structurally distinct chemical compounds and are unrelated to one another. These sequences are thus deemed to normally constitute independent and distinct inventions within the meaning of 35 U.S.C. 121.

Applicants wish to draw the Examiner's attention to the fact that while none of SEQ ID NOS:1-2128 contain sequences which are 100% identical to one another, there are sequences that are closely *related* to one another. Thus, there are sequences aside from SEQ ID NO:327 within SEQ ID NOS:1-2128 that fall within the scope of claim 97 which is drawn to an antibody that immunospecifically binds BLyS that comprises a first amino acid sequence at least 85% identical to amino acid residues 1-123 of SEQ ID NO:327 and a second amino acid sequence at least 85% identical to amino acid residues 139-249 of

SEQ ID NO:327. For example, SEQ ID NO:2, specifically recited in claim 101, has 7 amino acid differences compared to SEQ ID NO:327. More particularly, amino acids 1-123 of SEQ ID NO:2 is 95% identical to amino acids 1-123 of SEQ ID NO:327, and amino acids 139-249 of SEQ ID NO:2 is 99% identical to amino acids 139-249 of SEQ ID NO:327. An alignment of these two sequences is shown in Exhibit A.

MPEP § 803.04 provides for restriction between *unrelated* sequences. And while Applicants do not concede that sequences related to SEQ ID NO:327 and falling within the scope of claim 97 are unpatentable over one another, Applicants assert that these two sequences (and others within SEQ ID NOS:1-2128), are *related* to one another. Applicants submit that the purpose of the provisions of MPEP § 803.04 is not to permit restriction between sequences that are essentially close variants of one another, but rather to prevent the claiming of more than one distinct nucleotide sequence or protein sequence in one application for patent. Applicants hereby request that the sequence election be modified, so as to permit Applicants to specifically claim other disclosed sequences that fall within the scope of claim 97, such as for example, SEQ ID NO:2. It would not be an undue burden to allow Applicants to claim sequences so related to SEQ ID NO:327, because a search for antibodies that fall within the scope of claim 97 will necessarily encompass such related sequences. The matter of the undue search burden is addressed more fully in section (3) below.

*Newly added claims corresponding to original Markush claim 51 – Species election from species set E*

The Examiner has required an election of species from species set E corresponding to the members of the Markush group of claim 51. The members of the Markush group of original claim 51 corresponded to six discrete categories of antibody affinity. Newly added claims 107 and 124 corresponding to original Markush claim 51 are not presented as a Markush group and recite only one broader discrete range, *i.e.*, those wherein the antibody has a dissociation constant ( $K_D$ ) less than or equal to  $10^{-9}$ M. Effectively, newly added claims 107 and 124 contain only one species. Accordingly, Applicants submit that the revised format of claims 107 and 124 obviates the requirement for a species election from species set E

*Traversal of species election from species sets B-D and G<sup>3</sup> and traversal of the restriction of claims to one of Groups I-VI*

Applicants assert that the present restriction requirement is improper for the following reasons: (1) species elections within Markush-type claims have apparently been misapplied to claims other than the Markush-type; (2) generic claims are present and are improperly treated in the restriction requirement; and (3) it would not be a serious burden to search the inventions of the different groups together. A detailed discussion of these issues follows.

*(1) Species elections within Markush-type claims have been misapplied to claims other than the Markush-type claim<sup>4</sup>*

The Examiner has required an election of species from each set of species sets A-H for any elected Group, and an additional election of species from species set I if Applicants elected Group V or VI. Applicants submit that elections of species sets B-D are elections of species of Markush-type claims and that, as such, said species elections only apply to the Markush-type claims (claims 48-50 for species B-D, respectively). However, the Examiner's requirement that species elections A-H must be made if any one of Groups II-VI is elected leads Applicants to the understanding that the Examiner is applying these species election to claims other than the Markush type claims.

Applying the election of a species within a Markush type to claims to other than the Markush-type claim is improper because it reads limitations into the additional claims that are not there. In other words, if Applicants elect, for example, a human IgG1 constant domain from species set C, and the Examiner applies that election to all the claims within Elected Group I, that means the Examiner will examine the claims only insofar as the additional claims are drawn to antibody comprising an IgG1 heavy chain immunoglobulin constant domain. However none of the other claims in Group I, besides the claims that correspond to original claim 50 (claims 105, 122 and 139), either require implicitly or

<sup>3</sup> Applicants note that traversal of the species election requirement from species sets F and H have not been requested simply due to the fact that Applicants cancellation of the Markush claims 58 and 84, without addition of corresponding new claims. Reasons for not traversing, but rather requesting withdrawal of, species election from species set A were discussed above.

<sup>4</sup> Applicants only address species elections B-D in this section. Although a similar analysis would apply to the Examiner's requirement for an election of species from species set E, F and H as originally set forth in Paper No. 7, Applicants have cancelled the Markush-type claims associated with species sets F and H and have modified the claims corresponding to the Markush type claim of species set E (claim 51, now corresponding to new claims 107 and 124) such that they are no longer Markush-type claims. Therefore no election or arguments are presented here with regard to species sets E, F and H.

recite explicitly, the limitation that the antibody must contain an immunoglobulin constant domain, much less an IgG1 heavy chain immunoglobulin constant domain.

In this regard, the MPEP instructs that limitations may not be read into the claims which have no express basis in the claim. *See*, MPEP § 2111 ("The court explained that 'reading a claim in light of the specification, to thereby interpret limitations *explicitly* recited in the claim, is a quite different thing from 'reading limitations of the specification into a claim,' to thereby narrow the scope of the claim by implicitly adding disclosed limitations which have no express basis in the claim.'"). Section 2111 of the MPEP further instructs that proper examination requires that the pending claims be given the "broadest reasonable interpretation consistent with the specification.'...and broad interpretation by the Examiner reduces the possibility that the claim once issued, will be interpreted more broadly than is justified. *In re Prater* 415 F.2d 1393, 1404-5...(CCPA 1969)." Thus, Applicants submit that the Examiner's apparent application of species elections B-D to all the claims of Group I is improper and should only be applied to the newly added claims corresponding to each of Markush claims 48, 49 and 50 for each of species elections B, C and D, respectively, if the present restriction requirement is to be maintained<sup>5</sup>.

Moreover, Applicants wish to draw the Examiner's attention to MPEP § 803.02 which instructs that after election of a species in a Markush type claim,

[t]he Markush-type claim would then be examined fully with respect to the elected species and any species considered to be clearly unpatentable over the elected species....should no prior art be found that anticipates or renders obvious the elected species, the search of the Markush-type claim will be extended....The prior art search will be extended to the extent necessary to determine patentability of the Markush-type claim.

MPEP § 803.02 indicates that should the elected species of the Markush group be found allowable, that examination will be extended until at least one member of the Markush group is found not to be allowable or, alternatively, until all the members of the Markush group (and thus the entire Markush claim) are determined to be allowable. Thus, restriction of individual members of the Markush group does not result in withdrawal of the non-elected species from consideration by the Examiner unless at least one member of

<sup>5</sup> Applicants note that the election from species set G is not included in this discussion because the claims corresponding to original claims 60 and 61, (i.e. newly added claims 115, 116, 131 and 132) are not Markush claims. Nonetheless, reading the limitation of the species election from species set G to claims other than claims 115, 116, 131 and 132 would also be improper.

the Markush group is found not to be allowable over the prior art, and no rectifying amendment or convincing argument is made by the Applicant in response. Applicants submit that search of the restricted species together would not be an undue burden (see section (3) below) and that withdrawal of the restriction requirement, at least in so far as it applies to species elections B-D, would simplify and expedite examination of the present application.

In light of the above discussion, Applicants respectfully request that the Examiner reconsider and withdraw the requirement for a species election from each of species sets B-D. If the Examiner intends to maintain election from each of species sets B-D, Applicants request that, at the very least, the restriction requirement be modified to (1) clarify that these elections are species elections within a Markush type claim, applicable only to the newly added claims corresponding to Markush type claims 48, 49, and 50 (as identified in the chart above), and (2) to confirm that those claims will be examined according to the procedures set forth in MPEP §803.02.

(2) *Generic linking claims are present and are improperly treated in the restriction requirement*

At various points in the restriction requirement, different sets of claims are classified as generic. In paragraph 6, claims 1, 36, 43-84, and 87-96 are indicated as generic, while in paragraphs 7, 9, 10, 13, 15, and 19, it is stated that all claims (1-96) are generic. Further discrepancies can be found, for example in paragraph 17, in which claims 1-60 and 63-96 are classified as generic and in paragraph 21, in which claims 88-92 are classified as generic. Moreover paragraph 23, indicates that an argument in response to the restriction requirement that all claims are generic would be considered non-responsive, despite the fact that on six separate occasions the Examiner has indicated that all the claims are generic. Thus, Applicants are at a loss to understand which claims the Examiner considers generic and which claims he does not. It is important to correctly identify generic claims, because of the special treatment (described below) of generic claims with regard to restriction practice and examination.

MPEP § 806.04(d) defines a generic claim as follows (in pertinent part):

In general, a generic claim should include no material element additional to those recited in the species claims, and must comprehend within its confines the organization covered in each of the species.



For the purpose of obtaining claims to more than one species in the same case, the generic claim cannot include limitations not present in each of the added species claims. Otherwise stated, the claims to the species which can be included in a case in addition to a single species must contain all the limitations of the generic claim.

Once a claim that is determined to be generic is allowed, all of the claims drawn to species in addition to the elected species which include all the limitations of the generic claim will ordinarily be obviously allowable in view of the allowance of the generic claim, since the additional species will depend thereon or otherwise include all of the limitations thereof.

This last paragraph quoted above describes how the presence of a generic linking claim, if allowable, acts to prevent restriction between species. This concept is outlined further in MPEP §809.03 which states that:

There are a number of situations which arise in which an application has claims to two or more properly divisible inventions, so that requirement to restrict the application to one would be proper, but presented in the same case are one or more claims (generally called "linking" claims) inseparable therefrom and thus linking together the inventions otherwise divisible.

The most common types of linking claims which, if allowed, act to prevent restriction between inventions that can otherwise be shown to be divisible, are

- (A) genus claims linking species claims;
- (B) a claim to the necessary process of making a product linking proper process and product claims;
- (C) a claim to "means" for practicing a process linking proper apparatus and process claims; and
- (D) a claim to the product linking a process of making and a use (process of using).

Where linking claims exist, a letter including a restriction requirement only or a telephoned requirement to restrict (the latter being encouraged) will be effected, specifying which claims are considered to be linking. Examiners should use Form Paragraph 8.12 to make restrictions involving linking claims.

For example, original claim 1 is generic to original claims 2-73. This is because claims 2-73, each directly or indirectly dependent from claim 1, clearly contain all the limitations of the generic claim 1. Similarly, newly added claim 97 is a generic linking claim for claims 119-146. Arguments presented below for claim 1 would apply equally well to claim 97.

The Examiner's grouping of the generic or linking claim number 1 into Group I, fails to comply with MPEP §814 which states, in part, that:

*The generic or other linking claims should not be associated with any one of the linked inventions since such claims must be examined with any one of the linked inventions that may be elected. This fact should be clearly stated. (Emphasis added).*

A proper restriction requirement would have excluded claim 1 from any Group of claims and would have noted that claim 1 was generic to claims 2-73. Once a generic linking claim is properly identified, the MPEP § 809 states, in part, that:

*The linking claims must be examined with the invention elected, and should any linking claim be allowed, the restriction requirement must be withdrawn. Any claim(s) directed to the non-elected invention(s), previously withdrawn from consideration, which depends from or includes all the limitations of the allowable linking claim must be rejoined and will be fully examined for patentability. (Emphasis added).*

Therefore, pursuant to MPEP § 809, the generic linking claims (e.g., claim 1, if it were still pending, or newly added claim 97) should be examined with the elected group. Upon allowance of newly added claim 97, the present restriction of members of each species sets A-G would have to be withdrawn and the non-elected species from each of species sets A-G would have to be rejoined and examined for patentability.

A similar analysis would apply to original claim 60 which is a generic linking claim for original claims 61 and 62<sup>6</sup>. Applicants note that original claim 60 corresponds to new claims 114 and 131; original claim 61 corresponds to new claims 115 and 132; and original claims 62 corresponds to new claims 116 and 133. Upon allowance of either generic linking claim 114 or 131, the present species restriction would have to be withdrawn and the non-elected species in species set G (which would correspond to newly added claims 116 and 133) would have to be rejoined and examined for patentability.

In light of the above discussion, Applicants respectfully request that species election requirement from each of species sets B-D and G be reconsidered and withdrawn. If the Examiner intends to maintain election from each of species sets B-D and G, Applicants respectfully request that, at the very least, the restriction requirement

<sup>6</sup> Applicants note that while claim 60 is generic to claims 61 and 62, it is subgeneric to claim 1. Likewise, newly presented claim 101 is subgeneric to newly added claim 97, but claim 101 is generic to claims 136-146.

be modified to (1) acknowledge the presence of generic linking claim 97 and separate said generic linking claim out from Group I; (2) acknowledge that new claims 114 and 131 are generic to claims 115-116 and 132-133, respectively<sup>7</sup>, and (3) acknowledge that the allowance of a generic linking claim 97 would result in rejoinder and examination for patentability of all species from each of species sets B-D and G and that allowance of a [sub]generic linking claims 114 and 131 would result in rejoinder and examination for patentability of non-elected species in species set G<sup>8</sup>.

- (3) *It would not be a serious burden to search different groups or the different species within each of species sets B-D and G together*

MPEP § 803 instructs that, "[I]f the search and examination of an entire application can be made without serious burden, the Examiner must examine it on the merits, even though it includes claims to independent or distinct inventions." In the present situation, no such showing has been made aside from references to different classifications and assertions of being able to use the claimed products with different processes and *vice versa*. Applicants disagree that search of the groups together would be a serious burden and below provide arguments to support this assertion/premise.

*Search of the generic linking claim 97 is a search that must be performed no matter which Group is elected*

The search of generic claim 97 will entail a search for prior art antibodies that immunospecifically bind BLyS and a query as to whether any such antibodies contain amino acid sequences that are at least 85% identical to each of amino acids residues 1-123 and 139-249 of SEQ ID NO:327. It is necessary to perform this search no matter which species are elected or which group is elected, either because claim 97 is a generic linking claim (as it is for [most] claims within Group I) or because each of the claims in Groups II-VI in some way include the antibody of claim 97 as a material element.

<sup>7</sup> Additional subgeneric claims exist in the original and newly added claims. For example, as mentioned in footnote 3, claim 101 generic to claims 136-146. Also claim 108 is generic to claims 109-110; claim 11 is generic to claim 112, and claim 113 is generic to claims 114-118, etc. Applicants do not make an issue of these claims because the Examiner has not made these claims, or original claims corresponding to these claims, the subject of a species election requirement.

<sup>8</sup> Generally, if the generic linking claim is found to be allowable, then "all of the claims drawn to species in addition to the elected species ... will ordinarily be obviously allowable in view of the allowance of the generic claim, since the additional species will depend thereon or otherwise include all of the limitations thereof." See, MPEP § 806.04(d).

The search of the antibody of claim 97 is all that is necessary to allow examination of all the species, elected and non-elected. This is because the search of the antibody of generic linking claim 97 is a broader search than the search for individual species. If any art is found for claim 97, it would apply to all the species. If no art is found for claim 97, then all species should be allowable over the prior art, because each of the narrower claims containing species contain all the limitations of claim 97. If claim 97, is novel, so will all the species be novel (see, MPEP § 806.04(d)). Since the search for generic linking claim 97 encompasses all the searches necessary for the all the species, the combined search and examination of all species within species sets B-D and G would not entail a serious burden. Accordingly, Applicants respectfully request that the requirement for species elections from species sets B-D and G be reconsidered and withdrawn.

Furthermore, the search of the antibody of claim 97 will no doubt provide information regarding the existence of nucleic acid molecule encoding said antibody (Group II), cell lines expressing said antibody (Group III) and methods of using said antibody (Groups IV-VI). Thus, contrary to the Examiner's assertions at the end of paragraphs 25 and 26 of the restriction requirement, the searches for the different groups are clearly overlapping, if not co-extensive. Accordingly, Applicants respectfully request that the restriction requirement of the claims into Groups I-VI also be reconsidered and withdrawn.

### CONCLUSION

In view of the discussion above, Applicants respectfully repeat their request that the Examiner reconsider and withdraw the present restriction.

If, however, the Examiner insists on maintaining the restriction requirement, then Applicants respectfully request that the restriction requirement be modified according to one or more of the following:

- that the sequence election of SEQ ID NO:327 admits of express or implicit claiming of disclosed, related sequences or portions thereof that fall within the scope of newly added claim 97;
- that the requirement for a species election from species set A be withdrawn in light of its redundancy to the required sequence election;

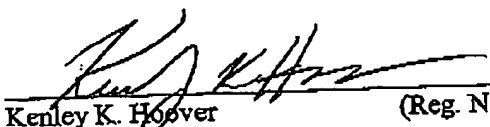
- that the requirement for a species election from each of species sets B-D, be recognized as species election within a Markush claim applicable only to the newly added claims corresponding to the original Markush claim and that such claims will be examined according to the provisions of in MPEP §803.02;
- that the requirement for a species election from species set E, be withdrawn in light of Applicants presentation of newly added claims (i.e. newly added claims 107 and 124) corresponding to original Markush claim 51 such that there is only one species claimed;
- that the requirement for a species election from species set G be modified to acknowledge that newly added claims 114 and 131 are generic linking claims linking the species recited in claims 115-116 and 132-133, respectively, and that allowance of linking claims 114 and 131 would result in rejoinder and examination for patentability of non-elected species in species set G; and/or
- that claim 97 be acknowledged as a generic linking claim 97 and separated out from Group I, and furthermore that it be acknowledged that the allowance of generic linking claim 97 would result in rejoinder and examination for patentability of all species from each of species sets B-D and G.

Applicants retain the right to petition from the restriction requirement under 37 CFR § 1.144 should the restriction requirement, either in its present form or in a modified form, be made final.

Applicants respectfully request that the above remarks be made of record in the file history of the instant application. If there are any fees due in connection with the filing of this paper, please charge the fees to our Deposit Account No. 08-3425. If a fee is required for an extension of time under 37 CFR § 1.136 that is not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,

Date: July 7, 2003

  
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Exhibit A

Alignment Report of 6D08 v 16A01.MEG, using Clustal method with PAM250 residue weight table. . Page 1  
Monday, July 07, 2003 12:20 PM

	10	20	30	40	50	
1	QVQLQQSGAEVKIKPGSSVRVSCKASGGTFNNNAINWVRQAPCGGLEWMGG					SEQ ID NO 2 6D08.PRO
1	QVQLQQSGAEVKIKPGSSVRVSCKASGGTFNNNAINWVRQAPCGGLEWMGG					SEQ ID NO 327 16A01.PRO
	60	70	80	90	100	
51	IIPMFGTAKYSONFQGRVAITADESTSTASMELSSLSRSEDVAVYYCARSR					SEQ ID NO 2 6D08.PRO
51	IIPMFGTAKYSONFQGRVAITADESTGTASMELSSLSRSEDVAVYYCARSR					SEQ ID NO 327 16A01.PRO
	110	120	130	140	150	
101	DLLEFPFYGMWGRGTMVTVSSGGGSGGGSGGGGSAFSSSELTQDPAV					SEQ ID NO 2 6D08.PRO
101	DLLEFPFHALSPWGRGTMVTVSSGGGSGGGSGGGGSAFSSSELTQDPAV					SEQ ID NO 327 16A01.PRO
	160	170	180	190	200	
151	SVALGQTVRVTCQGDLSRSTYASWYQKPGQAPVLIYGNKNNRPSGIPDR					SEQ ID NO 2 6D08.PRO
151	SVALGQTVRVTCQGDLSRSTYASWYQKPGQAPVLIYGNKNNRPSGIPDR					SEQ ID NO 327 16A01.PRO
	210	220	230	240		
201	PSGSSSGNTASLTITGAQAEDEADYYCNSRDSSGNHWVFGGGTELTVLG					SEQ ID NO 2 6D08.PRO
201	PSGSSSGNTASLTITGAQAEDEADYYCNSRDSSGNHWVFGGGTELTVLG					SEQ ID NO 327 16A01.PRO

Decoration 'Decoration #1': Shade (with solid black) residues that  
differ from SEQ ID NO 327 16A01.PRO.